Remarks

Claims 57-110 are pending in this application. Claims 57-78 and 105-110 are currently under examination. Claims 79-104 have been withdrawn as being directed to non-elected subject matter. Claims 57, 58, 77, and 78 have been amended. Claims 105-110 have been added.

Applicants have amended claims 57-58, 66, 69, 71, 72, and 76-78 to correct grammar or to make the claim language more clear.

New claims 105-110 have been added. Claims 105-106 are similar to claim 57. Claims 107-108 are similar to claim 77. Claims 109-110 are similar to claim 78. In addition, new claims 105-110 recite:

> the ***hydrophobic group*** is a C_1-C_{24} aliphatic moiety is selected from a saturated or unsaturated, branched or linear aliphatic chain, the aliphatic chain optionally containing an aliphatic ring, the aliphatic chain or ring optionally substituted with one or more substituents containing a heteroatom selected from the group consisting of oxygen, halogen, nitrogen and sulfur;

Support for this claim language appears in the specification and claims as originally filed. For example, please *see* claims 57, 77, and 78, and page 9, lines 4-13, of the present specification.

New claims 105-110 also recite:

> the ***protecting group*** is selected from the group consisting of methoxymethyl (MOM), tetrahydropyranyl (THP), diphenylmethyl, triethylsilyl (TES), *t*-butyldimethylsilyl (TBDMS), mesitoate, 9-fluorenylmethyl carbonate (f-moc) , t-butyl carbamate (t-boc), and $Si(R^5)_3$ wherein R^5 may be the same or different in the same moiety and is selected from a C_1-C_6 branched or straight alkyl group or an optionally substituted aryl group;

Support for this claim language appears in the specification and claims as originally

filed. For example, please *see* claims 57, 77, and 78, and page 10, lines 4-14 of the present specification.

New claims 105-110 also recite:

> the ***leaving group*** X is selected from the group consisting of a halogen atom, borate, ethylene chlorophosphite, methyl phosphodichloridite, chloro-N,N-diisopropylaminomethyxophosphite, and $[(isopropyl)_2N]_2POCH_2CH_2CN$, wherein X is optionally substituted with a group selected from the group consisting of an alcohol, an ether, a polyether, and a sugar moiety, wherein the alcohol contains an aliphatic moiety selected from an aliphatic chain, an amino aliphatic chain, a heteroatom comprising an aliphatic chain, an aliphatic chain comprising a cyclic ring which ring may be saturated or partially saturated, and an aryl group, the aliphatic chain may be a branched or straight, saturated or unsaturated chain.

Support for this claim language appears in the specification and claims as originally filed. For example, please *see* claims 57, 77, and 78, and page 9, line 25, to page 10, line 10, of the present specification.

New claims 106, 108, and 110 also recite that "provided R^1 represents a C_8-C_{24} aliphatic moiety; or Z represents a $Si(R^5)_3$ group in which R^5 may be the same or different in the same compound and represents a C_1-C_6 branched or straight alkyl group or an aryl group." Support for this claim language appears in the specification and claims as originally filed. For example, please *see* claims 59 and 64, page 9, lines 14-15, and page 10, lines 15-17, of the present specification.

Applicants, by cancelling or amending any claims herein, make no admission as to the validity of any rejection made by the Examiner against any of these claims. Applicants reserve the right to reassert any of the claims cancelled herein or the original claim scope of any claim amended herein, in a continuing application.

No new matter has been added. Applicants respectfully request entry of the amendments.

Applicants kindly acknowledge the Examiner's indication that claims 59, 64, 65, 67-69, and 76 are allowable if rewritten in independent format to include all of the recited features of the base claim and any intervening claim.

In view of the remarks set forth herein, further and favorable consideration is respectfully requested.

I. At page 2 of the Official Action, claims 5 and 6 have been rejected under 35 USC § 112, second paragraph.

The Examiner asserts that claims 57, 58, 60-63, 66, 70-75, 77, and 78 are indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. Specifically, the Examiner asserts that the recited hydrophobic group, protecting group, and leaving group "are not properly defined in the specification," and that the "metes and bounds of the claims are unclear."

Applicants respectfully traverse this rejection.

Applicants submit that the recited hydrophobic group, protecting group, and leaving group are well known art-recognized terms, and one of ordinary skill in the art reading the specification would understand the metes and bounds for each substituent recited in the claims.

"Leaving group" is recognized as a well known term of art, for example, please *see* http://www.chemicool.com/definition/leaving_group.html, "an atom or group (charged or uncharged) that becomes detached from an atom in what is considered to be the residual or main part of the substrate in a specified reaction. For example, in the

be the residual or main part of the substrate in a specified reaction. For example, in the heterolytic solvolysis of benzyl bromide in acetic acid."

"Protecting group" is recognized as a well known term of art, for example, please *see:* http://encarta.msn.com/dictionary_561533921/protecting_group.html, "atoms preventing unwanted reactions: a group of atoms that is added to a molecule in order to prevent existing groups in the molecule from undergoing unwanted chemical reactions. A protecting group can be easily attached to and removed from its target position without affecting the rest of the molecule."

"Hydrophobic group" is recognized as a well known term of art, for example, please *see*: http://dictionary.babylon.com/hydrophobic_(hydrophobicity;_hydrophobic_group), "a nonpolar molecule or group that has little affinity for water. Hydrophobic groups on molecules in solution tend to turn in on themselves or clump together with other hydrophobic groups because they are unable to disrupt the network of strong hydrogen bonds in the water around them."

In addition, Applicants submit that the recited art-recognized terms of hydrophobic group, protecting group, and leaving group are also distinctly described in the specification, and one of ordinary skill in the art reading the specification would understand the metes and bounds for each substituent recited in the claims.

"Leaving group" is distinctly described in the specification at page 9, line 25, to page 10, line 10. Accordingly, one of ordinary skill in the art reading the specification would understand that in combination with its art-recognized meaning the leaving group X may be selected from the group consisting of a halogen atom, borate, ethylene

chlorophosphite, methyl phosphodichloridite, chloro-N,N-diisopropylaminomethyxophosphite, and $[(isopropyl)_2N]_2POCH_2CH_2CN$, wherein X is optionally substituted with a group selected from an alcohol, an ether, a polyether, and a sugar moiety, wherein the alcohol contains an aliphatic moiety selected from an aliphatic chain, an amino aliphatic chain, a heteroatom comprising an aliphatic chain, an aliphatic chain comprising a cyclic ring which ring may be saturated or partially saturated, or an aryl group, the aliphatic chain may be a branched or straight, saturated or unsaturated chain.

"Protecting group" is distinctly defined in the specification at page 10, lines 4-14. Accordingly, one of ordinary skill in the art reading the specification would understand that in combination with its art-recognized meaning the protecting group may be selected from the group consisting of methoxymethyl (MOM), tetrahydropyranyl (THP), diphenylmethyl, triethylsilyl (TES), *t*-butyldimethylsilyl (TBDMS), mesitoate, 9-fluorenylmethyl carbonate (f-moc), t-butyl carbamate (t-boc), and $Si(R^5)_3$ wherein R^5 may be the same or different in the same moiety and is selected from a C_1-C_6 branched or straight alkyl group or an optionally substituted aryl group.

"Hydrophobic group" is distinctly described in the specification with reference to the definition of substituent R^2 at page 9, lines 4-13. Accordingly, one of ordinary skill in the art reading the specification would understand that in combination with its art-recognized meaning the hydrophobic group may be a C_1-C_{24} aliphatic moiety selected from a saturated or unsaturated, branched or linear aliphatic chain, the aliphatic chain optionally containing an aliphatic ring, the aliphatic chain or ring optionally substituted with one or more substituents containing a heteroatom selected from the group

consisting of oxygen, halogen, nitrogen and sulfur.

In view of the foregoing, it is submitted that claims 57, 58, 60-63, 66, 70-75, 77, and 78 are distinctly described within the meaning of 35 USC § 112, second paragraph. Newly added claims 105-110 specifically recite the above-noted descriptions of "leaving group," "protecting group," and "hydrophobic group," and therefore are also distinctly described within the meaning of 35 USC § 112, second paragraph. Accordingly, the Examiner is respectfully requested to withdraw this rejection.

II. At page 3 of the Official Action, claims 57, 58, 60-63, 66, 70-75, 77 and 78 have been rejected as obvious under 35 USC § 103(a) in view of:
DI: Deigner et al. Journal of Labeled Compounds and Radiopharmaceuticals, 34(2), 185 – 190 (1994).
D2: Deigner et al. Chemistry and Physics of Lipids, 61, 199-208 (1992).
D3: Lorene et al. Archiv Der Pharmazie, 319(11), 1023-1027 (1986).

Claims 57, 58, 60-63, 66, 70-75, 77 and 78 have been rejected as obvious under 35 USC § 103(a) in view of: Deigner et al., *Journal of Labeled Compounds and Radiopharmaceuticals*, 34(2), 185 – 190 (1994) ("D1"); Deigner et al., *Chemistry and Physics of Lipids*, 61, 199-208 (1992) ("D2"); and Lorene et al., *Archiv Der Pharmazie*, 319(11), 1023-1027 (1986) ("D3"). The Examiner asserts that the "claimed compound of the general formula 1 is a homolog of the prior art compounds," that "homologs are obvious," and that "one of ordinary skill in the art would have a reasonable expectation of success in practicing the instant invention by varying the substituents on the oxazaphospholane ring to arrive at the instantly claimed oxazaphospholane compounds." *See* the Official Action at pages 5-6.

In view of the following these rejections are respectfully traversed.

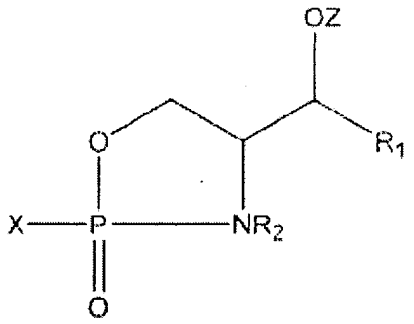
The U.S. Supreme Court in *Graham v. John Deere Co.*, 148 U.S.P.Q. 459 (1966) held that non-obviousness was determined under 35 USC § 103 by: (1) determining the scope and content of the prior art; (2) ascertaining the differences between the prior art and the claims at issue; (3) resolving the level of ordinary skill in the art; and, (4) inquiring as to any objective evidence of non-obviousness.

Furthermore, to establish a prima facie case of obviousness, the Examiner must satisfy three requirements. First, as the U.S. Supreme Court very recently held in *KSR International Co. v. Teleflex Inc. et al.,* Slip Opinion No. 04–1350, 550 U. S. ____ (April 30, 2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (*KSR*, supra, slip opinion at 13-15.) Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ2d 1016, 1023 (Fed. Cir. 1991). Lastly, the prior art

references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

After *KSR*, the Federal Circuit in *Takeda Chemical Industries v. Alphapharm*, 492 F.3d 1350, 84 USPQ2d 1197 (Fed. Cir. 2007), has applied the teaching, suggestion, motivation (TSM) test after *KSR*. The Appellant in this declaratory judgment action argued that the claimed chemical compound was an obvious modification of a previously known compound. *Id.* at 1353. The Federal Circuit rejected this, holding that "in cases involving new chemical compounds, it remains necessary to identify some reasons that would have led a chemist to modify a known compound in a particular manner to establish *prima facie* obviousness of a new claimed compound." *Id.* at 1357. Notably, the Court also rejected the Appellant's "obvious to try" argument, as the Appellant failed to demonstrate that one of ordinary skill would have chosen the prior art compound to modify from the millions of possibilities. *Id.* at 1360.

The present claimed subject matter relates to oxaphospholane compounds of formula (1):



wherein

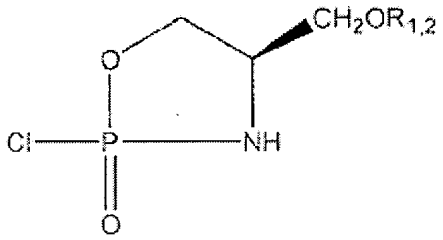
R^1 represents a C_1-C_{24} aliphatic moiety which may be saturated or unsaturated, branched or linear chain, optionally containing an aliphatic ring;

R^2 represents a hydrogen atom or hydrophobic group;

Z represents a protecting group; and

X represents a leaving group.

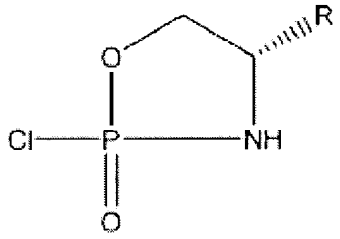
As also noted by the Examiner, **D1** describes a compound having the general formula (see page 186):



wherein

R_1 and R_2 are either a C_{10} or C_{16} alkyl radical.

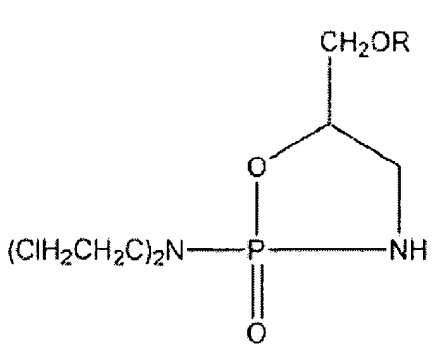
D2 describes a compound having the general formula (see page 200):

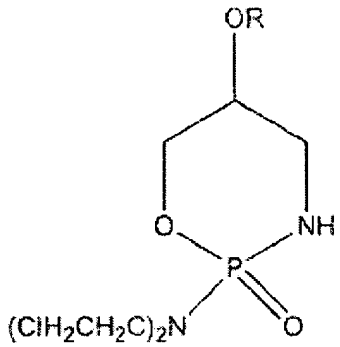


wherein

R may be an ester (-$COOC_5H_{11}$, -$COOC_6H_{17}$), an alkyl (-$(CH_2)_3CH_3$), or an ether (-$CH_2OC_6H_{17}$, –CH_2-O-$C_{10}H_{21}$).

With respect to **D3**, the Examiner refers to a five and even six membered oxazaphospholane compounds of the general formulae:





wherein R may be a C_6-C_7 alkyl radical.

DI, D2, and D3 provide a oxazaphospholane compound containing a ***single substituent at position 4 (position 5 for D3), that is a non-branched substituent, such as a linear alkoxy, ester, ether, alkyl, aryl, or arylalkyl*** .

Primarily, ***the present claimed subject matter provides an alkyl of C_2-C_{25} at position 4, that is substituted with the –OZ group at the first carbon atom nearest the ring***. There is no teaching or suggestion in the combination of cited documents to provide for –OZ substitution at this position, wherein Z is a protecting group.

Also, ***the six membered ring of D3, and the substitution at position 5, is completely different from the five membered ring recited in the present claims***. Any conclusion drawn with respect to a six membered ring cannot be automatically deduced for a five membered ring.

Applicants submit that under current US case law (*Takeda vs. Alpharma*), similar chemical compounds have been found to be non-obvious over prior art compounds, and are not *prima facie* obvious under the obviousness standards described in *KSR vs. Teleflex*. In this case, there is no teaching, suggestion, or motivation to modify the general chemical genus described in any of the cited documents with one or more

synthetic modifications to devise the claimed chemical genus of formula (I), including the required –OZ group substituted on an alkyl substituted at position 4 of the recited ring structure. Even if one did try these modifications, Applicants argue that because of unpredictability in the art there is still no reasonable expectation of successfully achieving the claimed compounds without undue experimentation.

Moreover, relevant case law holds that the generic disclosure of a chemical invention may not, depending on the facts, invalidate or render the species unpatentable. *See In re Baird*, 16 F.3d 380, 29 U.S.P.Q.2d 1550 (Fed. Cir. 1994); *In re Jones*, 958 F.2d 347, 21 U.S.P.Q.2d 1941 (Fed. Cir. 1992).

The invention in *Baird* covered a flash fusible toner comprising a polyester of bisphenol A and an aliphatic dicarboxylic acid. The Board affirmed the examiner's obviousness rejection on grounds that the prior art reference specifically described compositions comprising esters of three dicarboxylic acids claimed and a generic diphenol formula that encompassed bisphenol A. Although Baird argued that the reference lacked motivation to select bisphenol A, the Board disagreed, concluding that the generic disclosure of the reference provided ample motivation to select the claimed bisphenol A polyester binder resin in arriving at the claimed composition. *In re Baird*, 16 F.3d at 382, 29 U.S.P.Q.2d at 1551.

In *Baird*, the Federal Circuit reversed the obviousness determiniation of the Board, holding that a generic formula does not by itself necessarily render a compound encompassed by that formula obvious. *In re Baird*, 16 F.3d at 382, 29 U.S.P.Q.2d at 1552. Noting that the generic formula of the diphenol encompassed more than 100 million different diphenols, the court found no suggestion in the reference to select the

particular combination of variables in that formula that would give rise to bisphenol A. Indeed, as the court observed, the reference appeared to teach away from using bisphenol A by focusing on more complex diphenols as "preferred" or "optimum." *Id.* at 382-83, 29 U.S.P.Q.2d at 1552.

Emphasizing that one must evaluate a reference "not only for what it expressly teaches, but also for what it fairly suggests," the Federal Circuit in *Baird* considered the vast number of diphenols encompassed by the generic diphenol of the reference, coupled with the clear preference for diphenols other than that claimed by Baird, and concluded that the prior art did "not teach or fairly suggest the selection of bisphenol A." *Id.* at 383, 29 U.S.P.Q.2d at 1552. The court therefore determined that the Board clearly erred in holding Baird's claimed compound obvious under § 103.

Applying *Baird* in the present case, the chemical structures in the cited documents do not teach or fairly suggest the selection of the claimed species of a oxazaphospholane compound comprising an alkyl of C_2-C_{25} at position 4, that is substituted with an –OZ group at the first carbon atom nearest the ring.

In addition, the combination of art cited by the Examiner does not teach or suggest each and every element of the presently claimed subject matter since the Examiner has not provided any reference disclosing the -OZ group. This is further evidence that there is lack of a reasonable expectation of success in preparing the presently claimed compounds, as the substitution required by the present claims is not even recognized in the art.

Furthermore, regarding whether structural homology is evidence of a prima facie case of obviousness, **MPEP 2144.09** states that the presence or absence of a prior art

suggestion of method of making a claimed compound may be relevant in determining *prima facie* obviousness. ***"[I]f the prior art of record fails to disclose or render obvious a method for making a claimed compound, at the time the invention was made, it may not be legally concluded that the compound itself is in the possession of the public***. In this context, we say that the absence of a known or obvious process for making the claimed compounds overcomes a presumption that the compounds are obvious, based on the close relationships between their structures and those of prior art compounds." Citing *In re Hoeksema*, 399 F.2d 269, 274-75, 158 USPQ 597, 601 (CCPA 1968).

In the present claimed subject matter, one of the substituents is an oxygen protected with a group Z (protecting group), to be removed at a later stage of the process. ***This protecting group Z is required in order to prevent the reaction of the oxygen atom in any further reactions of the oxazaphospholane compound***. In contrast, Applicants note that none of the documents D1-D3 attempt to solve a problem of a vulnerable hydroxyl moiety (or any other such functional groups) in an oxazaphospholane ring, to be used in the synthesis of other derivatives. Accordingly, there is no teaching or suggestion in the combination of cited documents to provide a method for a protecting group Z in order to prevent the reaction of the oxygen atom in any further reactions of the oxazaphospholane compound during the production of the claimed compound.

Thus, Applicants submit that a person skilled in the art at the time of filing would not have been motivated to use the disclosure in any one of D1, D2, or D3, taken alone or in combination, in order to arrive at a compound of the present claimed subject

matter. Moreover, one of ordinary skill in the art would not have had a reasonable expectation of successfully deriving the claimed compounds from the combination of cited references for at least the reason that they would not have predictably expected that a Z protecting group would have been required to achieve the claimed compounds.

For the same reasons provided above, newly added claims 105-110 are nonobvious over the cited prior art. In addition, Applicants note that newly added claims 106, 108, and 110 specifically recite

> provided R^1 represents a C_8-C_{24} aliphatic moiety; or
> Z represents a $Si(R^5)_3$ group in which R^5 may be the same or different in the same compound and represents a C_1-C_6 branched or straight alkyl group or an aryl group.

These are the same features recited in claims 59 and 64, which have been deemed allowable by the Examiner. Accordingly, for at least this additional reason, claims 106, 108, and 110 are also nonobvious over the cited prior art.

The compounds of the present application are thus nonobvious over the cited prior art under 35 USC § 103(a). Thus, the Examiner is respectfully requested to withdraw this rejection as to claims 57, 58, 60-63, 66, 70-75, 77 and 78.

Conclusion

In view of the foregoing, Applicant submits that the application is in condition for immediate allowance. Early notice to that effect is earnestly solicited. The Examiner is invited to contact the undersigned attorney if it is believed that such contact will expedite the prosecution of the application.

In the event this paper is not timely filed, Applicants petition for an appropriate extension of time. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

THE NATH LAW GROUP

Date: January 23, 2009

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